Bayer

Bayer Corporation
100 Bayer Road
Pittsburgh, PA 15205-9741
Phone: 412 777-2000

November 14, 2003

Honorable Marianne Lamont Horinko
Acting Administrator
U.S. Environmental Protection Agency
c/o P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program
Re: HPV Registration No.

Dear Administrator Horinko;

Bayer Chemicals Corporation LLC (Bayer) is pleased to submit the proposed test plan along with the current robust summaries in IUCLID format for Benzyltrimethylammonium chloride (CAS# 56-93-9).

Cynthia Graham, Ph.D. is our technical contact and can be reached at 412-777-3933 or by email at cynthia.graham@bayerpolymers.com .

This submission is also being sent electronically to the following e-mail addresses:
Oppt.ncic@epa.gov
Chem.rtk@epa.gov

Sincerely,

Janet M. Mostowy, Ph.D.
Vice President
Product Safety & Regulatory Affairs

Enclosures: Test Plan, IUCLID data set on CAS# 56-93-9

cc: R. Hefter
O. Hernandez
K. Hoffman
M. Josephic

Benzyltrimethylammonium chloride

CAS # 56-93-9

Test plan justification

Bayer Chemicals LLC

November 14, 2003

Executive Summary

Bayer Chemicals LLC (Bayer) hereby submits for review and public comment their test plan for Benzyltrimethylammonium chloride (CAS# 56-93-9) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program.

IUPAC Name	Abbreviation	CAS#
N,N,N-trimethyl-benzenemethanaminium chloride	BTMAC	56-93-9

BTMAC is used as:

A solvent for cellulose; a gelling inhibitor in polyester resins; an intermediate (Lewis, RJ 1997); a dye assistant for acrylics (Syracuse Research Institute); and a Phase-transfer agent (Ashford, R.D. 1994).

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of low concern for aquatic toxicity, low concern as Persistent Organic Pollutants, and of high concern for mammalian toxicity. Bayer concludes that there is sufficient, reliable data on BTMAC except for Developmental toxicity. **An OECD 414 study is recommended for fulfilling the endpoints of the HPV Program.**

Data Review

Physicochemical properties:

The properties of BTMAC can be found in Handbooks such as Hawley's Condensed Chemical Dictionary. BTMAC is a liquid at ambient temperatures, with a freezing point of -50ºC and boiling point and decomposition temperature of 135ºC. The measured octanol/water partition coefficient is -2.17 and it is highly soluble in water. A calculation for vapor pressure resulted in 0.0000000308 hPa (0.0000000231mm Hg) at 25ºC. Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

BTMAC was calculated to have a photodegradation half-life of 7.4 hours. Fugacity modeling demonstrates partitioning to the soil and water compartments, negligible amounts to air and sediment. A biodegradation study demonstrated that BTMAC and other quaternary ammonium compounds are not readily biodegradable and at high concentrations may be toxic to the microbial sludge. However, acclimation profoundly influences the biodegradability and therefore these compounds should not be considered persistent. BTMAC is very stable in water, confirmed by the marketed product being an aqueous solution. No additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

Aquatic studies have been performed on the aquatic invertebrate, *Daphnia pulex* and two species of algae. *Daphnia* appear to be the most sensitive species: LC_{50}= 11.94 mg/l as compared to 14 day EC_0 of *Anabaena variabilis* and *Oscillatoria* species of 1857 mg/l. There are no studies on fish, however ECOSAR estimates that fish are less sensitive than *Daphnia* or algae. Therefore an additional animal study would not provide additional information that would be useful or relevant. No additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Acute toxicity studies show that BTMAC is toxic by the oral route of exposure in rats (LD_{50} = 180 mg/kg). Acute toxicity of BTMAC was characterized by severe cholinergic symptoms including salivation, chromodacryorrhea, and sedation. (See Table 1 and IUCLID document).

There are multiple studies to fill the Mutagenicity endpoints, both *in vitro* and *in vivo*. Ames results were consistently negative; a chromosome aberration study using Chinese hamster lung cells was ambiguous; and an *in vivo* mouse micronucleus test

revealed a positive increase in micronuclei that was significantly different from the control only the highest dose tested (100 mg/kg). (See Table 1 and IUCLID document).

There are several repeated dose toxicity studies (28 day and 90 day) by the oral route of exposure in rats and mice. A NOAEL of 25 mg/kg/day was determined. Some cholinergic effects including chromodacryorrhea, lacrimation, salivation, pupillary constriction, altered gait, and mild tremors were observed at non-lethal doses (See Table 1 and attached IUCLID document).

At the end of the 90 day study, in both rats and mice, samples were collected for sperm motility and vaginal cytology evaluations. No treatment-related differences were detected in reproductive tissue evaluations or estrous cycle characterizations, except in female rats where a minimal shortening of diestrus and prolongation of proestrus occurred in the 25 mg/kg females with no alteration in the length of the estrous cycle. There was no Developmental study located, therefore an OECD 414 is proposed. (See Table 1 and attached IUCLID document).

There is data to cover all SIDS endpoints, except for Developmental toxicity. An OECD 414 study is recommended for fulfilling the endpoints of the HPV Program (See Table 2).

Conclusion

Existing data indicates that this chemical is of low concern for aquatic toxicity, low concern as Persistent Organic Pollutants, and high concern for mammalian toxicity. Bayer concludes that there is sufficient, reliable data on BTMAC except for Developmental toxicity. An OECD 414 study is recommended for fulfilling the endpoints of the HPV Program.

Table 1. Available data for BTMAC (CAS# 56-93-9)

Endpoint	Result	Method/Reference*
Physical-Chemical Data		
Melting Point	-50º C	Handbook value
Boiling Point	> 135º C	Handbook value
Vapour Pressure	0.0000000308 hPa	MPBPWin v1.41
Partition Coefficient ($logP_{ow}$)	-2.17	Hansch & Leo, 1995
Water Solubility	Highly soluble	Handbook value
Environmental Fate		
Photodegradation	½ life = 7.4 hours	AOPWin calculation
Fugacity	Air = < 0.1% Water = 45.3% Soil = 54.6% Sediment = < 0.1%	EPIWin Fugacity Level III calculation
Biodegradability	0% after 10 days	Urano & Katz, 1986
Water Stability	stable	Sold as an aqueous solution
Ecotoxicology		
Acute Fish Toxicity (96 hrs)	No data	
Acute Invertebrate Toxicity (48 hrs)	LC50 = 11.94 mg/l	EPA OPP 72-2
Algal Toxicity (14 days)	LC0 = 1875 mg/l	Rucka, et al., 1980
Mammalian Toxicology		
Acute Toxicity	180 mg/kg bw (oral, rat)	Sanders, et al., 1995
Mutagenicity	negative	Ames
Chromosome Aberration	Ambiguous positive	Chinese Hamster lung cells Mouse micronucleus test
Repeated Dose Toxicity	NOAEL = 25 mg/kg/day (Rat and mouse, oral, 90 days)	EPA OPP 82-1
Reproductive Toxicity	No adverse effects on reproductive organs (Rat and mouse, oral, 90 days)	EPA OPP 82-1
Developmental Toxicity	No data	

* Robust summaries and References can be found in the IUCLID document.

Table 2. Test Plan for BTMAC (CAS# 56-93-9)

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	
Boiling Point	✓	✓	
Vapour Pressure			
Partition Coefficient ($logP_{ow}$)	✓	✓	
Water Solubility	✓	✓	
Environmental Fate			
Photodegradation	✓	✓	
Fugacity	✓	✓	
Biodegradability	✓	✓	
Water Stability	✓	✓	
Ecotoxicology			
Acute Fish Toxicity			Derogation statement: less sensitive species
Acute Invertebrate Toxicity	✓	✓	
Algal Toxicity	✓	✓	
Mammalian Toxicology			
Acute Toxicity	✓	✓	
Mutagenicity	✓	✓	
Chromosome Aberration	✓	✓	
Repeated Dose Toxicity	✓	✓	
Reproductive Toxicity	✓	✓	
Developmental Toxicity			OECD 414

✓ = data available and considered adequate.

References

Ashford, R.D. 1994. Ashford's Dictionary of Industrial Chemicals. London, England: Wavelength Publications Ltd., 1994. 124

Hansch C, Leo A, and Hoekman D. 1995. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society. p.79.

Lewis, RJ Sr (Ed.). 1997. Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 133.

Rucka M, Oswiecimska M, et al. 1980. New Biocides for Cooling Water Treatment. Environ. Protection Engin. 6(4):455-464.

Sanders JM, Griffin RJ, Burka LT, and Matthews HB. 1995. Toxicokinetics of the cholinomimetic compound benzyltrimethylammonium chloride in the male rat and mouse. Xenobiotica. 25(3):303-313.

Urano, K and Katz Z. 1986. Evaluation of Biodegradation Ranks of Priority Organic Compounds. J. Haz. Mat. 13:147-159.

Additional References can be found in the IUCLID document.

201-14845B

I U C L I D

Data Set

Existing Chemical	:	ID: 56-93-9
CAS No.	:	56-93-9
EINECS Name	:	benzyltrimethylammonium chloride
EC No.	:	200-300-3
Molecular Formula	:	C10H16N.Cl

Producer related part

Company	:	Bayer Corporation
Creation date	:	29.05.2003

Substance related part

Company	:	Bayer Corporation
Creation date	:	29.05.2003
Status	:	
Memo	:	
Printing date	:	11.11.2003
Revision date	:	
Date of last update	:	11.11.2003
Number of pages	:	28
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Bayer Corporation
Contact person	:	
Date	:	
Street	:	100 Bayer Road, Building #5
Town	:	PA 15205-9741 Pittsburgh
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

14.08.2003

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	CN(C)(C)(Cc1ccccc1)CL
Molecular formula	:	C10 H16 CL1 N1
Molecular weight	:	185.70
Petrol class	:	

23.10.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	liquid
Purity	:	60 - % v/v
Colour	:	white to light yellow
Odour	:	slight almond
Remark	:	sold as an aqueous solution

30.10.2003

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

BTMAC

23.10.2003

N,N,N-trimethyl-benzenemethanaminium chloride

30.10.2003

trimethylbenzylammonium chloride

23.10.2003

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	< -50 °C
Sublimation	:	
Method	:	other: Handbook
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data from Handbook or collection of data
Flag	:	Critical study for SIDS endpoint

30.10.2003 (1)

2.2 BOILING POINT

Value	:	> 135 °C at
Decomposition	:	yes
Method	:	other: Handbook
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Above 135 degree C, the substance decomposes to benzyl chloride and trimethylamine.
Reliability	:	(2) valid with restrictions Data from Handbook or collection of data
Flag	:	Critical study for SIDS endpoint

30.10.2003 (1)

2.3 DENSITY

Type	:	relative density
Value	:	1.07 at 20 °C
Method	:	other: Handbook
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data from Handbook or collection of data
Flag	:	Critical study for SIDS endpoint

27.10.2003 (1)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	.0000000308 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated): MPBPWIN v1.41
Year	:	
GLP	:	no

Test substance	:	other TS: molecular structure of Benzyl trimethyl ammonium chloride
Result	:	SMILES : CN(C)(C)(Cc1ccccc1)CL CHEM : Benzyl trimethyl ammonium chloride MOL FOR: C10 H16 CL1 N1 MOL WT : 185.70 Vapor Pressure Estimations (25 deg C): (Using BP: 409.99 deg C (estimated)) (Using MP: 239.00 deg C (exp database)) VP: 4.04E-009 mm Hg (Antoine Method) VP: 2.31E-008 mm Hg (Modified Grain Method) VP: 7.46E-008 mm Hg (Mackay Method) Selected VP: 2.31E-008 mm Hg (Modified Grain Method)
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

30.10.2003 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	-2.17 at 25 °C
pH value	:	
Method	:	other (measured)
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment.
Flag	:	Critical study for SIDS endpoint

23.10.2003 (3)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Description	:	of high solubility
Stable	:	
Deg. product	:	
Method	:	other: Handbook
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	very soluble; sold as an aqueous solution
Reliability	:	(2) valid with restrictions Data from Handbook or collection of data
Flag	:	Critical study for SIDS endpoint

11.11.2003 (1)

Solubility in	:	Water
Value	:	> 1 - vol% at °C
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

11.11.2003 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm?
Rate constant	:	.0000000000173 cm³/(molecule*sec)
Degradation	:	50 % after 7.4 hour(s)
Deg. product	:	
Method	:	other (calculated): AOP Program (v1.91)
Year	:	
GLP	:	no
Test substance	:	other TS: molecular structure of Benzyl trimethyl ammonium chloride
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

30.10.2003 (2)

3.1.2 STABILITY IN WATER

Type	:	abiotic
Remark	:	Sold as an aqueous solution.
Flag	:	Critical study for SIDS endpoint

29.10.2003

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	other: air - water - soil - sediment
Method	:	other: EPIWIN version 3.11
Year	:	2000
Remark	:	Modeling was performed using equal releases (300 kg/hr) and equal distribution to all compartments.
Result	:	

	Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
Air	1.09e-005	14.8	300
Water	45.3	360	300
Soil	54.6	360	300
Sediment	0.0755	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (%)	Advection (%)
Air	5.44e-017	0.0194	0.00414	0.000215	4.6e-005
Water	1.56e-018	330	172	36.7	19.1
Soil	6.94e-017	398	0	44.2	0
Sediment	1.30e-018	0.138	0.00572	0.0153	0.000635

Persistence Time: 421 hr
Reaction Time: 520 hr
Advection Time: 2.21e+003 hr
Percent Reacted: 80.9
Percent Advected: 19.1

Reliability : (2) valid with restrictions
Accepted calculation method

Flag : Critical study for SIDS endpoint

30.10.2003 (2)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: sludge (30 mg/l)
Concentration : 100 mg/l related to Test substance
related to
Contact time : 28 day(s)
Degradation : 1 (±) % after 28 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment

11.11.2003 (4)

Type : aerobic
Inoculum : activated sludge
Concentration : 100 mg/l related to Test substance
related to
Contact time : 10 day(s)
Degradation : 0 (±) % after 10 day(s)
Result : under test conditions no biodegradation observed
Deg. product :
Method :
Year :
GLP : no data
Test substance : no data

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment

Flag : Critical study for SIDS endpoint
11.11.2003 (5)

Type : aerobic
Inoculum :

Remark : Studies on the influence of chemical structure on the biodegradability of quaternary ammonium compounds (QACs) suggest that few, if any, should be regarded as persistent, although at high concentrations they may be toxic to the microbial population. Alkyl trimethylammonium QACs will be most rapidly degraded followed by alkyldimethylbenzylammonium and alkylpyridinium QACs. The acclimation of the microbial community profoundly influences the biodegradability of QACs.
Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag : Critical study for SIDS endpoint
11.11.2003 (6)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species :
Exposure period : 42 day(s) at °C
Concentration : 2 mg/l
BCF : < .2
Elimination :
Method : other
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

11.11.2003 (4)

Species :
Exposure period : 42 day(s) at °C
Concentration : .2 mg/l
BCF : < 1.5
Elimination :
Method : other
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

11.11.2003 (4)

Species : other
Exposure period : at °C
Concentration :
BCF : 3.16
Elimination :
Method : other: BCF Program (v2.15)
Year : 2000
GLP : no
Test substance : other TS: molecular structure of Benzyl trimethyl ammonium chloride

Result : ---------- Bcfwin v2.15 ----------
Log Kow (estimated) : -2.47
Log Kow (experimental): -2.17
Log Kow used by BCF estimates: -2.17

Equation Used to Make BCF estimate:
Log BCF = 0.50 (Ionic; Log Kow dependent)

Estimated Log BCF = 0.500 (BCF = 3.162)

Reliability : (2) valid with restrictions
Accepted calculation method

11.11.2003 (2)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type :
Species :
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : > 1000
Method : other
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Flag : Critical study for SIDS endpoint
11.11.2003 (4)

Type : other
Species :
Exposure period :
Unit :
Method : other: ECOSAR v0.99g
Year :
GLP : no
Test substance : other TS: molecular structure of Benzyl trimethyl ammonium chloride

Remark : Fish are the least sensitive aquatic species.
Result : MOL FOR: C10 H16 CL1 N1
MOL WT : 185.70
Log Kow: -2.47 (KowWin estimate)
Melt Pt:
Wat Sol: 2.994E+007 mg/L (calculated)

ECOSAR v0.99g Class(es) Found

Neutral Organics

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organic SAR: Fish (Baseline Toxicity)		14-day	LC50	1.95e+006
Neutral Organics:	Fish	96-hr	LC50	2.19e+006
Neutral Organics:	Fish	14-day	LC50	1.95e+006
Neutral Organics:	Daphnid	48-hr	LC50	1.72e+006
Neutral Organics:	Green Algae	96-hr	EC50	8.33e+005

11.11.2003 (2)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia pulex (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 11.94
Analytical monitoring : no data
Method : EPA OPP 72-2
Year :
GLP : no data

Test substance	:	other TS: commercial product BTMAC (quaternary benzyl trimethyl ammonium chloride 60%)
Method	:	According to: Peltier WH and Weber CW. 1985. EPA/600/4-85/013. Environmental Monitoring and Support Laboratory. Cincinnati, OH p.216
Remark	:	Data were analyzed using the trimmed Spearman-Karber method (Hamilton, MA, et al., 1977. Environ. Sci. & Technol. 11:714.
Result	:	LC50 = 11.94 ppm (6.94 - 16.94 ppm)
Test condition	:	Dilution water hardness = 25-40 mg/l as CaCO3; Dissolved oxygen = 3.7 - 7.5 ppm pH = 7-8 Temperature = 20-21 degree C
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag	:	Critical study for SIDS endpoint

30.10.2003 (7)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Anabaena variabilis (Algae)
Endpoint	:	biomass
Exposure period	:	14 day(s)
Unit	:	mg/l
NOEC	:	1857
EC0	:	1857
Limit test	:	
Analytical monitoring	:	no data
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: benzyltrimethylammonium chloride; purity >98%
Method	:	Tests for algacidal activity were performed with a nutrient solution of (in g/dm3): KNO3 = 0.5; KH2PO4 = 0..2; MgSO4.7H2O = 0.16; FeC6H5O7 = 0.003; (OH)C3H4(COOH)3 = 0.03; and microelements. Nutrient solution (48 ml), the appropriate concentration of test substance, and 2 ml of homogenized suspension of algae were combined in a flask and the optical density determined. There were 5 replicates per test substance; 20 replicates per control. The flasks were incubated in a thermolumino-state at 20 degree C for 14 days. The content of chlorophyll (in biomass) was determined according to "Standard Methods for Examination of Water and Wastewater, 14th edition. American Public Health Association, Inc. New York. 1975." The percent inhibition was calculated, assuming the chlorophyll content of the controls was 100%.
Remark	:	Mean value of chlorophyll (control): 0.62 mg
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag	:	Critical study for SIDS endpoint

29.10.2003 (8)

Species	:	Oscillatoria sp. (Algae)
Endpoint	:	biomass
Exposure period	:	14 day(s)
Unit	:	mg/l
NOEC	:	1857
EC0	:	1857

Limit test	:	
Analytical monitoring	:	no data
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: benzyltrimethylammonium chloride; purity >98%
Method	:	Tests for algacidal activity were performed with a nutrient solution of (in g/dm3): KNO3 = 0.5; KH2PO4 = 0..2; MgSO4.7H2O = 0.16; FeC6H5O7 = 0.003; (OH)C3H4(COOH)3 = 0.03; and microelements. Nutrient solution (48 ml), the appropriate concentration of test substance, and 2 ml of homogenized suspension of algae were combined in a flask and the optical density determined. There were 5 replicates per test substance; 20 replicates per control. The flasks were incubated in a thermolumino-state at 20 degree C for 14 days. The content of chlorophyll (in biomass) was determined according to "Standard Methods for Examination of Water and Wastewater, 14th edition. American Public Health Association, Inc. New York. 1975." The percent inhibition was calculated, assuming the chlorophyll content of the controls was 100%.
Remark	:	Mean value of chlorophyll (control): 0.59 mg
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag	:	Critical study for SIDS endpoint

29.10.2003 (8)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	180 mg/kg bw
Species	:	rat
Strain	:	Fischer 344
Sex	:	male
Number of animals	:	5
Vehicle	:	water
Doses	:	125, 175, 210, 250 mg/kg
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: Benzyltrimethylammonium chloride; purity not noted; purchased from Aldrich Chemical Company, Milwaukee, WI
Method	:	BTMAC was administered by gavage at desired concentrations in dose volumes of 5ml/kg. Each rat concurrently received a subcutaneous injection of either saline, neostigmine (0.1 mg/kg), or atropine sulphate (1.0 mg/kg) in a dose volume of 1 ml/kg. Each rat was closely observed for muscarinic type cholinergic symptoms (salivation and chromodacryorrhea), respiratory difficulties, convulsions, and death. The Reed-Muench method (1938) was used to maximize lethality data.
Result	:	Acute toxicity of BTMAC was characterized by severe cholinergic symptoms including salivation, chromodacryorrhea, and sedation. Diarrhea, tremors, clonic convulsions, and respiratory distress were also usually present. Death or survival of each animal was generally determined within 3 hours of dosing. The various concurrent treatments did not alter the lethality of BTMAC since mortality was identical for each of the dose groups.
Reliability	:	(2) valid with restrictions Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag	:	Critical study for SIDS endpoint

30.10.2003 (9)

Type	:	LD50
Value	:	250 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: According to DeWitt et al. 1953
Year	:	
GLP	:	
Test substance	:	other TS: Benzyltrimethylammonium chloride; purity not noted

23.10.2003 (10)

Type	:	LD100
Value	:	1600 mg/kg bw
Species	:	mouse
Strain	:	other: TAC:SWfBr

Sex	:	male
Number of animals	:	
Vehicle	:	physiol. saline
Doses	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: Benzyltrimethylammonium chloride; purity not noted; purchased from Aldrich Chemical Company
Method	:	The test substance was suspended in saline and administered orally to non-fasted male mice. The animals were held in cages for 72 hours and deaths recorded. The LD50 values were calculated using the Litchfield and Wilcoxin method.
Remark	:	Gastrocnemius muscle twitch response: maximum change = 10.1% at 25 mg/kg

30.10.2003 (11)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	13 week
Frequency of treatm.	:	5 days/week
Post exposure period	:	
Doses	:	0, 12.5, 25, 50, 100 mg/kg
Control group	:	yes, concurrent vehicle
NOAEL	:	25 mg/kg bw
Method	:	EPA OPP 82-1
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The minimally toxic dose (MTD) was estimated to be 50 mg/kg. BTMAC had little effect on the body weights of rats or mice, final mean weights were within 8% (rats) or 3% (mice) of control animals. The deaths

of 2 female rats and one mouse of each sex administered 100 mg/kg were the result of pharmacologic effects on the cardiovascular system. Some cholinergic effects including chromodacryorrhea, lacrimation, salivation, pupillary constriction, altered gait, and mild tremors were observed at non-lethal doses. No significant target organ toxicity was observed in dosed rats or mice.

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

30.10.2003 (12)

Type : Sub-chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 13 week
Frequency of treatm. : 5 days/week
Post exposure period :
Doses : 0, 12.5, 25, 50, 100 mg/kg
Control group : yes, concurrent vehicle
NOAEL : 25 mg/kg
Method : EPA OPP 82-1
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : The minimally toxic dose (MTD) was estimated to be 50 mg/kg.
BTMAC had little effect on the body weights of rats or mice, final mean weights were within 8% (rats) or 3% (mice) of control animals. The deaths of 2 female rats and one mouse of each sex administered 100 mg/kg were the result of pharmacologic effects on the cardiovascular system. Some cholinergic effects including chromodacryorrhea, lacrimation, salivation, pupillary constriction, altered gait, and mild tremors were observed at non-lethal doses. No significant target organ toxicity was observed in dosed rats or mice.

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

30.10.2003 (12)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : other: Crj:CD (SD)
Route of admin. : oral unspecified
Exposure period : 28 days
Frequency of treatm. :
Post exposure period : 15 days
Doses : 0, 30, 60, 120 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL : 30 mg/kg bw
NOEL (female) : 60 mg/kg bw
Method : other: Guidelines for 28-day Repeated Dose Toxicity Testing of Chemicals (Japan)
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : 5 animlas/sex/group
Result : NOEL (males) = 30 mg/kg/day
NOEL (females) = 60 mg/kg/day

Observations:
60 mg/kg/day group:
Increased salivation (males)
120 mg/kg/day group:
Increased salivation (males and females)
Increased lacrimation and soiled fur (males and females)
Increased piloerection (females)
Suppression of body weight gain (males)
Decreased food consumption (males)
Hematology: increased Hgb, MCV, and MCH levels (males)

One female in high dose group died during the 4th week of the dosing period. Histopathology of the deceased animal revealed hepatocellular swelling and eosinophilic bodies.

Test substance : purity = 98%
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
30.10.2003 (13)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimurium TA100, TA1535, TA98, TA1537; Escherichia coli WP2uvrA
Test concentration : 156, 313, 625, 1250, 2500, 5000 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: Guidelines for Screening Mutagenicity of Chemicals (Japan)
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Test condition : solvent: distilled water
positive controls:
AF-2 for TA100, TA98, E. coli WP2 uvrA (non-activated);
sodium azide for TA1535 (non-activated);
9-aminoacridine for TA1537 (non-activated);
2-aminoanthracene for all strains (activated)
S9 metabolic activation:
rat liver induced with phenobarbital and 5,6-benzoflavone
3 plates/test; 2 replicates
Test substance : purity > 99%
Reliability : (1) valid without restriction
GLP Guideline study
Flag : Critical study for SIDS endpoint
15.08.2003 (13)

Type : Chromosomal aberration test
System of testing : Chinese hamster lung cells
Test concentration : up to 1900 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result : ambiguous
Method : other: Guidelines for Screening Mutagenicity of Chemicals (Japan)
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result	:	Genetic effects: without activation: clastogenicity = negative; polyploidy = negative with activation: clastogenicity =ambiguous; polyploidy = negative This chemical slightly increased incidences of structural chromosomal aberrations with an exogenous metabolic activation system. Clear reproducibility was obtained in the confirmatory study.
Test condition	:	solvent: physiological saline doses: 475, 950, 1900 ug/ml (+/- S9 activation) (confirmatory test) 1000, 1300, 1600, 1900 ug/ml (+S9) S9 = rat liver induced with phenobarbital and 5,6-benzoflavone all concentrations run in duplicate
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

27.10.2003 (13)

Type	:	Salmonella typhimurium reverse mutation assay
System of testing	:	Salmonella typhimurium TA 97, TA98, TA 100, TA 1535
Test concentration	:	up to 10000 ug/plate
Cycotoxic concentr.	:	> 10000 ug/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	EPA OPPTS 870.5265
Year	:	
GLP	:	no data
Test substance	:	other TS: benzyltrimethylammonium chloride (CAS# 56-93-9) purchased from Pfaltz & Bauer; purity not noted
Test condition	:	Salmonella typhimurium strains were obtained from Dr. Bruce Ames, University of California, Berkeley. Metabolic activation (S-9 fractions) obtained from Aroclor-induced, male Sprague-Dawley rat and male Syrian hamster livers. All strains were tested without metabolic activation, with 10% S-9 and 30% S-9.
Conclusion	:	The chemical was judged to be non-mutagenic in all strains, at all doses tested, both with and without metabolic activation.
Reliability	:	(1) valid without restriction Guideline study

24.10.2003 (14)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 97, TA98, TA 100, TA 1535
Test concentration	:	up to 10000 ug/plate
Cycotoxic concentr.	:	> 10000 ug/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	EPA OPPTS 870.5265
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Each trial consisted of triplicate plates of concurrent positive and negative controls and five doses of BTMAC. The metabolic activation enzymes and co-factors were obtained from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster livers. In this assay, a positive response is defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response is defined as a non-reproducible, non dose-related increase. A negative response is obtained when no increase in revertant colonies is observed following chemical treatment.
Reliability	:	(1) valid without restriction

GLP Guideline study

24.10.2003 (12)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	gavage
Exposure period	:	13 weeks
Doses	:	0, 12.5, 25, 50, or 100 mg/kg
Result	:	positive
Method	:	
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	At the end of the 13 week study, peripheral blood samples were obtained from male and female mice. Smears were immediately prepared and fixed in absolute methanol. The fixed slides were stained with acridine orange and coded. Slides were scanned to determine the frequency of micronulei in 1,000 normochromatic erythrocytes (NCEs) in up to 10 animals per dose group. The results were tabulated as the mean of pooled results from all animals within a treatment group (plus or minus the standard error of mean). The frequency of micronucleaeted cells per NCEs was analyzed with a one-tailed Cochran-Armitage trend test, followed by pairwise comparisons between each dose group and the control group. An individual trial is considered positive if the trend test P value is equal to or less than 0.025 or if the P value for any single dose group is equal to or less than 0.025 divided by the number of dose groups.
Result	:	Micronucleus analyses yielded positive trends ($P \leq 0.025$) for both male and female data, but only the highest dose tested (100 mg/kg) produced an increase in micronuclei that was significantly different from the control frequency ($P \leq 0.006$).
Reliability	:	(1) valid without restriction GLP Guideline study
Flag	:	Critical study for SIDS endpoint

30.10.2003 (12)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other: reproductive organ examination in 13 week study
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	5 days/ week

No. of generation studies	:	
Doses	:	0, 25, 50, 100 mg/kg
Control group	:	yes, concurrent vehicle
Method	:	other: EPA OPP 82-1
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : At the end of the 13 week study, samples were collected for sperm motility and vaginal cytology evaluations on rats and mice receiving 0, 25, 50, or 100 mg/kg. Methods used are described in NTP's sperm morphology and vaginal cytology evaluations protocol (NTP, 1991).
For 12 consecutive days prior to scheduled terminal sacrifice, the vaginal vaults of the female animals were moistened with saline, if necessary, and samples of fluid and cells were stained. Relative numbers of leukocytes, nucleated epithelial cells, and large squamous epithelial cells were determined and used to ascertain estrous cycle stage, length of estrous cycle, and percentage of cycle spent in estrous.
The left testis, left epididymis, and left caudal epididymis of male animals were isolated, weighed, and evaluated for spermatid heads per testis and per gram testis; spermatid counts; and epididymal spermatozoal motility and concentration.

Result : There were no differences in reproductive tissue parameters in males. A minimal shortening of diestrus and prolongation of proestrus occurred in the 25 mg/kg females. There was no alteration in the length of the estrous cycle.

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

30.10.2003 (12)

Type	:	other: reproductive organ examination in 13 week study
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	5 days/ week
No. of generation studies	:	
Doses	:	0, 25, 50, 100 mg/kg
Control group	:	yes, concurrent vehicle
Method	:	other: EPA OPP 82-1
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : At the end of the 13 week study, samples were collected for sperm motility and vaginal cytology evaluations on rats and mice receiving 0, 25, 50, or 100 mg/kg. Methods used are described in NTP's sperm morphology and vaginal cytology evaluations protocol (NTP, 1991).
For 12 consecutive days prior to scheduled terminal sacrifice, the vaginal vaults of the female animals were moistened with saline, if necessary, and samples of fluid and cells were stained. Relative numbers of leukocytes, nucleated epithelial cells, and large squamous epithelial cells were determined and used to ascertain estrous cycle stage, length of estrous cycle, and percentage of cycle spent in estrous.

The left testis, left epididymis, and left caudal epididymis of male animals were isolated, weighed, and evaluated for spermatid heads per testis and per gram testis; spermatid counts; and epididymal spermatozoal motility and concentration.

Result : No treatment-related differences were detected in reproductive tissue evaluations or estrous cycle characterizations.

Reliability : (1) valid without restriction
GLP Guideline study

Flag : Critical study for SIDS endpoint

30.10.2003 (12)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT